Supplemental Information

Antibodies

A mouse monoclonal antibody to C9neo (Hycult, Canton, MA) that recognizes a neoepitope on the complement component C9 integrated in the membrane attack complex (MAC) was used at 1:50; a rabbit polyclonal antibody to the C_{5b-9} complex (Abcam, Cambridge, MA) that also labels the MAC, was used at 1:750. A mouse monoclonal antibody against the complement component C3 (Novus, Littleton, CO) that plays a central role in the activation of both the classical and alternative pathways was used at 1:100. In serial sections of the tumors we used a chicken polyclonal antibody against the microtubule associated protein-2 (MAP2) (Covance, Berkeley, CA) at 1:5000, to demonstrate neurons and dendritic processes. In brain tissue samples we used antibodies against lymphocyte subpopulations: CD3 (Leica, Bannockburn, IL) at 1:100; CD4 (Biocare, Concord, CA) at 1:20; CD8 at 1:20, CD20 at 1:250; and CD138 (plasma cells/plasmablasts) at 1:50 (CD138), the last three from Dako, Carpinteria, CA.

Immunocytochemistry with cultured rat hippocampal neurons

Embryonic rat hippocampal neurons were cultured as previously described.[e4] 21 days *in vitro* rat hippocampal neurons were incubated with patients' or control CSF and 5% fresh normal human serum (NHS) as a source of complement. Additional controls included replacement of fresh NHS by heat inactivated NHS (56^{o} C for 30 minutes) or 1% bovine serum albumin (BSA) in phosphate buffered saline (PBS).

In brief, non-permeabilized live neurons were first incubated with CSF (1:20) of patients or controls for 1 hour at 37ºC, washed with PBS, and then incubated with NHS (1:20), heat-

inactivated NHS or 1% BSA for 30 minutes at 37ºC. After washing, neurons were fixed in 4% paraformaldehyde and sequentially incubated with anti-complement antibodies (C3, $C_{5b-9,}$ C9neo) for 30 min at 4°C, and the appropriate species Alexa Fluor secondary antibody (1:1500, Molecular Probes, Eugene, OR) for 45 minutes on ice. Coverslips were mounted using mounting media for fluorescence (Vector, Burlingame CA) containing DAPI (1.5 μg/ml). The binding of patients' antibodies and complement were photographed under a fluorescence microscope using Zeiss Axiovision software (Zeiss, Thornwood, NY).

Binding of antibodies and complement to cultured neurons

Cultures of hippocampal neurons treated with patients' CSF and a source of complement (5% NHS) showed intense immunolabeling of the cell surface and neuronal processes by NMDAR antibodies (supplemental Figure 1 A and G) and linear deposits of complement components C3, $C_{5b-9,}$ C9neo on the cell membrane of 90% of neurons (supplemental Figure 1 B). Similar studies with CSF from individuals used as control (stroke, non-inflammatory degenerative disease) were negative for antibody binding (supplemental Figure 1 E), but 5% of neurons showed mild complement staining in the absence of antibody binding (data not shown). No complement was detected on neurons treated with patients' CSF and heat-inactivated NHS or 1% BSA (supplemental Figure 1 H).